

10/528,612 - ~~418~~ 371

I. Process 1-3 Form I

II. Comp Form II 4

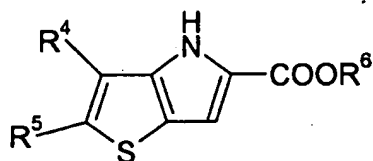
III. Process Form II 5

IV. Compound Form II 6

Amendments to the Claims:

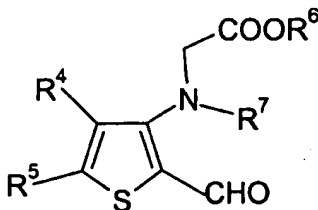
This listing of claims will replace all prior versions, and listings, of claims in the application.

1. (currently amended) A process for preparing a compound of formula (I)



(I)

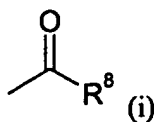
where R^4 and R^5 are independently selected from hydrogen, halo, nitro, cyano, hydroxy, fluoromethyl, difluoromethyl, trifluoromethyl, trifluoromethoxy, amino, carboxy, carbamoyl, mercapto, sulphamoyl, ureido, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{1-6} alkoxy, C_{1-6} alkanoyl, C_{1-6} alkanoyloxy, N -(C_{1-6} alkyl)amino, N,N -(C_{1-6} alkyl) $_2$ amino, C_{1-6} alkanoylamino, N -(C_{1-6} alkyl)carbamoyl, N,N -(C_{1-6} alkyl) $_2$ carbamoyl, C_{1-6} alkylS(O) $_a$ wherein a is 0 to 2, C_{1-6} alkoxycarbonyl, C_{1-6} alkoxycarbonylamino, N -(C_{1-6} alkyl)sulphamoyl, N,N -(C_{1-6} alkyl) $_2$ sulphamoyl, C_{1-6} alkylsulphonylamino and C_{1-6} alkylsulphonyl- N -(C_{1-6} alkyl)amino; and R^6 is hydrogen or a protecting group, which process comprises cyclisation of a compound of formula (II)



(II)

where R^4 , R^5 and R^6 are as defined in relation to formula (I), and R^7 is a nitrogen protecting group[[.]]; and removing the group R^7 [[.]]; and thereafter if desired, optionally removing any protecting group R^6 .

2. (original) A method according to claim 1 wherein R^7 is a group of sub-formula (i)

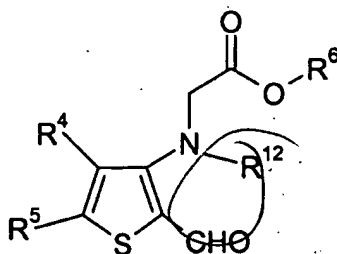


where R^8 is a straight chain alkyl group of from 1 to 6 carbon atoms.

3. (original) A process according to claim 1 or claim 2 wherein R^4 and R^5 are independently selected from hydrogen, halo, nitro, cyano, fluoromethyl, difluoromethyl, trifluoromethyl, trifluoromethoxy, carboxy, carbamoyl, sulphamoyl, ureido, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{1-6} alkoxy, C_{1-6} alkanoyl and C_{1-6} alkanoyloxy.

4. (original) A compound of formula (II) as defined in claim 1.

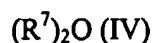
5. (original) A process for preparing a compound according to claim 4 which comprises reacting a compound of formula (III)



(III)

where R^4 and R^5 are as defined in relation to formula (I), and R^{12} is a directing nitrogen protecting group,

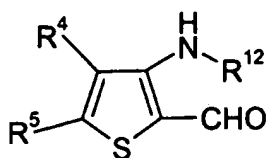
with a compound of formula (IV)



where R^7 is as defined above, under acidic conditions.

6. (original) A compound of formula (III) as defined in claim 5.

7. (original) A process for preparing a compound according to claim 6 which comprises reacting a compound of formula (V)



(V)

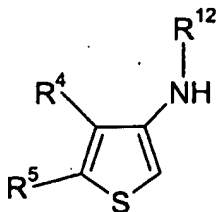
where R^4 and R^5 are as defined above in claim 1 and R^{12} is as defined in relation to formula (III),
with a compound of formula (VI)



where L is a leaving group.

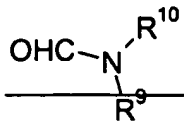
8. (original) A compound of formula (V) as defined in claim 7.

9. (currently amended) A process for preparing a compound according to claim 8 which
comprises reacting a compound of formula (VII)



(VII)

where R^4 and R^5 are as defined in claim 1 and R^{12} is as defined in relation to formula (III),
with a lithiating agent, ~~such as *N*-butyl lithium~~, and subsequently with a formylating agent[[,]]
~~such as a compound of formula (VIII)~~

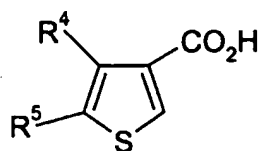


(VIII)

where R^9 and R^{10} are alkyl groups and in particular lower alkyl groups of 1 to 4 carbon atoms,
such as methyl.

10. (original) A compound of formula (VII) as defined in claim 9.

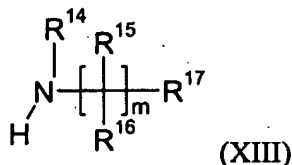
11. (original) A process for preparing a compound according to claim 10 which comprises subjecting a compound of formula (IX)



(IX)

where R^4 and R^5 are as defined above in relation to formula (I),
to a Curtius rearrangement reaction, in the presence of an alcohol of formula $R^{12}OH$ where R^{12} is as defined in claim 5.

12. (currently amended) A ~~method~~ process according to claim 1, for ~~the production of~~ preparing a compound of formula (I) where R^6 is hydrogen, wherein the method further comprises the step of reacting the compound of formula (I) obtained with an amine of formula (XIII)[[,]]



(XIII)

where R^{14} is selected from hydrogen or C_{1-8} alkyl,

m is an integer of from 0 to 4,

each R^{15} is the same or different and is selected from hydrogen, halo, nitro, cyano, hydroxy, amino, carboxy, carbamoyl, mercapto, sulphamoyl, ureido, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{1-6} alkoxy, C_{1-6} alkanoyl, C_{1-6} alkanoyloxy, N -(C_{1-6} alkyl)amino, N,N -(C_{1-6} alkyl) $_2$ amino, C_{1-6} alkanoylamino, N -(C_{1-6} alkyl)carbamoyl, N,N -(C_{1-6} alkyl) $_2$ carbamoyl, C_{1-6} alkylS(O) $_a$ wherein a is 0 to 2, C_{1-6} alkoxycarbonyl, C_{1-6} alkoxycarbonylamino, N -(C_{1-6} alkyl)sulphamoyl, N,N -(C_{1-6} alkyl) $_2$ sulphamoyl, C_{1-6} alkylsulphonylamino, C_{1-6} alkylsulphonyl- N -(C_{1-6} alkyl)amino, C_{3-8} cycloalkyl, C_{3-8} cycloalkyl C_{1-6} alkyl, aryl, aryl C_{1-6} alkyl, heterocyclic group and (heterocyclic group) C_{1-6} alkyl; wherein R^+ R^{15} may be optionally substituted on carbon by one or more

groups selected from P and wherein if said heterocyclic group contains an -NH- moiety that nitrogen may be optionally substituted by a group selected from R;

each R¹⁶ is the same or different and is selected from hydrogen or C₁₋₆alkyl;

R¹⁷ is selected from hydrogen, halo, nitro, cyano, hydroxy, fluoromethyl, difluoromethyl, trifluoromethyl, trifluoromethoxy, amino, carboxy, carbamoyl, mercapto, sulphamoyl, ureido, C₁₋₆alkyl, C₂₋₆alkenyl, C₂₋₆alkynyl, C₁₋₆alkoxy, C₁₋₆alkanoyl, C₁₋₆alkanoyloxy, *N*-(C₁₋₆alkyl)amino, *N,N*-(C₁₋₆alkyl)₂amino, C₁₋₆alkanoylamino, *N*-(C₁₋₆alkyl)carbamoyl, *N,N*-(C₁₋₆alkyl)₂carbamoyl, *N*-(C₁₋₆alkyl)-*N*-(C₁₋₆alkoxy)carbamoyl, C₁₋₆alkylS(O)_a wherein a is 0 to 2, C₁₋₆alkoxycarbonyl, C₁₋₆alkoxycarbonylamino, *N*-(C₁₋₆alkyl)sulphamoyl, *N,N*-(C₁₋₆alkyl)₂sulphamoyl, sulphamoylamino, *N*-(C₁₋₆alkyl)sulphamoylamino, *N,N*-(C₁₋₆alkyl)₂sulphamoylamino, C₁₋₆alkylsulphonylamino, C₁₋₆alkylsulphonylaminocarbonyl, C₁₋₆alkylsulphonyl-*N*-(C₁₋₆alkyl)amino and a group -E-F-G-H;

wherein E and G are independently selected from a direct bond, -O-, -S-, -SO-, -SO₂-, -OC(O)-, -C(O)O-, -C(O)-, -NR^a-, -NR^aC(O)-, -C(O)NR^a-, -SO₂NR^a-, -NR^aSO₂-, -NR^aC(O)NR^b-, -OC(O)NR^a-, -NR^aC(O)O-, -NR^aSO₂NR^b-, -SO₂NR^aC(O)- and -C(O)NR^aSO₂-; wherein R^a and R^b are independently selected from hydrogen or C₁₋₆alkyl which is optionally substituted by a group V;

F is C₁₋₆alkylene optionally substituted by one or more Q or a direct bond;

H is selected from aryl, C₃₋₈cycloalkyl and heterocyclic groups; wherein H may be optionally substituted on carbon by one or more groups selected from S and wherein if said heterocyclic group contains an -NH- moiety that nitrogen may be optionally substituted by a group selected from T;

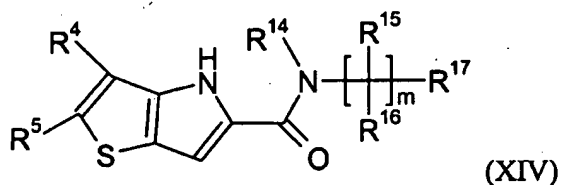
P, S and Q are independently selected from halo, nitro, cyano, hydroxy, trifluoromethyl, trifluoromethoxy, amino, carboxy, carbamoyl, mercapto, sulphamoyl, ureido, C₁₋₆alkyl, C₂₋₆alkenyl, C₂₋₆alkynyl, C₁₋₆alkoxy, C₁₋₆alkanoyl, C₁₋₆alkanoyloxy, *N*-(C₁₋₆alkyl)amino, *N,N*-(C₁₋₆alkyl)₂amino, C₁₋₆alkanoylamino, *N*-(C₁₋₆alkyl)carbamoyl, *N,N*-(C₁₋₆alkyl)₂carbamoyl, *N*-(C₁₋₆alkyl)-*N*-(C₁₋₆alkoxy)carbamoyl, C₁₋₆alkylS(O)_a wherein a is 0 to 2, C₁₋₆alkoxycarbonyl, C₁₋₆alkoxycarbonylamino, *N*-(C₁₋₆alkyl)sulphamoyl, *N,N*-(C₁₋₆alkyl)₂sulphamoyl, C₁₋₆alkylsulphonylamino, C₁₋₆alkylsulphonyl-*N*-(C₁₋₆alkyl)amino, C₃₋₈cycloalkyl, aryl and heterocyclic group;

wherein P, S and Q may be optionally and independently substituted on carbon by one or more groups selected from V and wherein if said heterocyclic group contains an -NH- moiety that nitrogen may be optionally substituted by a group selected from U;

V is selected from halo, nitro, cyano, hydroxy, trifluoromethoxy, trifluoromethyl, amino, carboxy, carbamoyl, mercapto, sulphamoyl, methyl, ethyl, methoxy, ethoxy, acetyl, acetoxy, methylamino, ethylamino, dimethylamino, diethylamino, *N*-methyl-*N*-ethylamino, acetylamino, *N*-methylcarbamoyl, *N*-ethylcarbamoyl, *N,N*-dimethylcarbamoyl, *N,N*-diethylcarbamoyl, *N*-methyl-*N*-ethylcarbamoyl, methylthio, ethylthio, methylsulphinyl, ethylsulphinyl, mesyl, ethylsulphonyl, methoxycarbonyl, ethoxycarbonyl, *N*-methylsulphamoyl, *N*-ethylsulphamoyl, *N,N*-dimethylsulphamoyl, *N,N*-diethylsulphamoyl, *N*-methyl-*N*-ethylsulphamoyl, morpholino, morpholinocarbonyl, *N*-benzylcarbamoyl, and 4-hydroxypiperidinocarbonyl;

R, T and U are independently selected from C₁₋₄alkyl, C₁₋₄alkanoyl, C₁₋₄alkylsulphonyl, C₁₋₄alkoxycarbonyl, carbamoyl, *N*-(C₁₋₄alkyl)carbamoyl, *N,N*-(C₁₋₄alkyl)carbamoyl, phenyl, benzyl, benzyloxycarbonyl, benzoyl and phenylsulphonyl wherein R, T and U may be optionally and independently substituted on carbon by one or more groups selected from V;

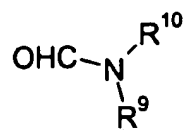
~~to produce~~ producing a compound of formula (XIV)



where R⁴, R⁵, R¹⁵, R¹⁶, R¹⁷ and m are as defined above,

or a pharmaceutically acceptable salt or an *in vivo* hydrolysable ester thereof.

13. (new) The process of claim 9, wherein the formylating agent is a compound of formula (VIII)



(VIII)

where R^9 and R^{10} are alkyl groups.

14. (new) The process of claim 13, wherein one or both of R^9 and R^{10} are lower alkyl groups.
15. (new) The process of claim 14, wherein one or both of R^9 and R^{10} are methyl groups